

Indolinone Combinational Libraries and Related Products  
and Methods for the Treatment of Disease

Abstract

5 The present invention relates to organic molecules  
capable of modulating, regulating and/or inhibiting  
protein kinase signal transduction. Such compounds are  
useful for the treatment of diseases related to  
unregulated protein kinase signal transduction, including  
cell proliferative diseases such as cancer,  
10 atherosclerosis, arthritis and restenosis and metabolic  
diseases such as diabetes. The present invention features  
indolinone compounds that potently inhibit protein kinases  
and related products and methods. Inhibitors specific to  
the *FLK* protein kinase can be obtained by adding chemical  
15 substituents to the 3-[(indole-3-yl)methylene]-2-  
indolinone, in particular at the 1' position of the indole  
ring. Indolinone compounds that specifically inhibit the  
*FLK* and platelet derived growth factor protein kinases can  
harbor a tetrahydroindole or cyclopentano-b-pyrrol moiety.  
20 Indolinone compounds that are modified with substituents,  
particularly at the 5 position of the oxindole ring, can  
effectively activate protein kinases. This invention also  
features novel hydrosoluble indolinone compounds that are  
tyrosine kinase inhibitors and related products and  
25 methods.